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Assistant Commissioner for PatentsUS SN 09/719,870

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

REMARKS

Claims 1-30 are now in the application.

The above amendment is submitted with respect to Claims 1-30 that were filed with the International Authority on April 20 and August 29, 2000.

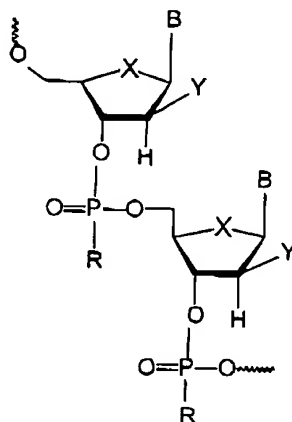
No new matter is believed to be introduced herewith.

Applicants believe that the present invention particularly as claimed herein, defines subject matter that is entitled to patent protection in the United States. Accordingly, an early and favorable action on the merits is believed to be appropriate and is courteously solicited.

In the event that there are any questions concerning this amendment, or application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Version with markings to show changes made

1. (Amended) A composition to selectively prevent gene transcription and expression in a sequence-specific manner; which comprises an effective amount of at least one selected from the group consisting of an oligonucleotide consisting essentially of arabinose sugars hybridizing to a single stranded RNA to induce RNase H activity; an oligonucleotide consisting essentially of arabinose sugars substituted at 2' position of the sugar ring with halogen, alkyl, alkylhalide, alkylsulfhydryl, allyl, amino, aryl, alkoxy, or azido and hybridizing to duplex DNA/DNA or DNA/RNA to form a triple helical complex, in association with an acceptable carrier.
2. (Amended) The composition of claim 1, wherein said oligonucleotide has the formula:



wherein,

B is selected from the group consisting of adenine, guanine, uracil, thymine, cytosine, inosine, and 5-methylcytosine;

Y at the 2' position of the sugar ring is selected from the group consisting of a halogen (fluorine, chlorine, bromine, iodine), ~~hydroxyl~~, alkyl, alkylhalide (e.g., -CH₂F), alkylsulfhydryl (-SCH₃), allyl, amino, aryl, alkoxy, and azido;

R at the internucleotide phosphate linkage is selected from the group consisting of oxygen, sulfur, methyl, amino, alkylamino, dialkylamino (the alkyl group having one to about 20 carbon atoms), methoxy, and ethoxy; and

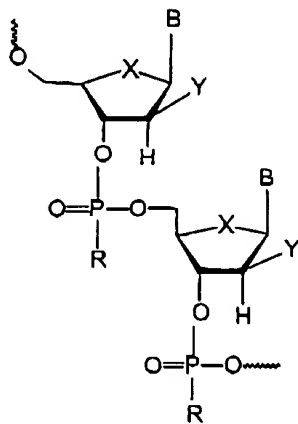
X at the furanose ring (position 4') is selected from the group consisting of oxygen, sulfur, and methylene (CH₂).

4. (Amended) The composition of claim 1 ~~or~~ 2, wherein said RNA is complementary RNA.

6. (Amended) The composition of claims 1-5, wherein said acceptable carrier is a pharmaceutically acceptable carrier for administration to a host.

8. (Amended) A method to inhibit DNA replication and/or DNA transcription, which comprises hybridizing in a sequence specific manner an oligonucleotide consisting essentially of arabinose sugars substituted at 2' position of the sugar ring with halogen, alkyl, alkylhalide, alkylsulfhydryl, allyl, amino, aryl, alkoxy, or azido to duplex DNA/DNA or DNA/RNA to form a triple helical complex; thereby inhibiting DNA replication and/or DNA transcription.

9. (Amended) The method of claim 7 ~~or~~ 8, wherein said oligonucleotide has the formula:



wherein,

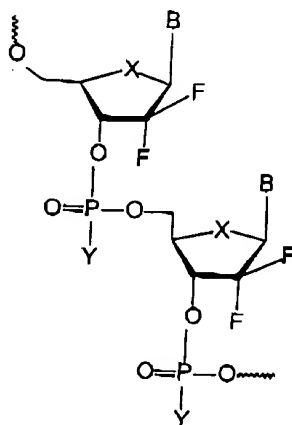
B is selected from the group consisting of adenine, guanine, uracil, thymine, cytosine, inosine, and 5-methylcytosine;

Y at the 2' position of the sugar ring is selected from the group consisting of a halogen (fluorine, chlorine, bromine, iodine), ~~hydroxyl~~, alkyl, alkylhalide (e.g., -CH₂F), alkylsulfhydryl (-SCH₃), allyl, amino, aryl, alkoxy, and azido;

R at the internucleotide phosphate linkage is selected from the group consisting of oxygen, sulfur, methyl, amino, alkylamino, dialkylamino (the alkyl group having one to about 20 carbon atoms), methoxy, and ethoxy; and

X at the furanose ring (position 4') is selected from the group consisting of oxygen, sulfur, and methylene (CH₂).

10. (Amended) The method of claim 7 ~~or~~ 8, wherein said oligonucleotide is



wherein,

B is selected from the group consisting of adenine, guanine, uracil, thymine, cytosine, inosine, 5-methylcytosine;

Y at the internucleotide phosphate linkage is selected from the group consisting of oxygen, sulfur, methyl, amino, alkylamino, dialkylamino (the alkyl group having one to about 20 carbon atoms), methoxy, and ethoxy; and

X at the furanose ring (position 4') is selected from the group consisting of oxygen, sulfur, and methylene (CH₂).

11. (Amended) The method of claim 7 ~~or 8~~ wherein said oligonucleotide is chemically modified at least at one site with a ligand or a pharmacological agent to enhance at least one of: (i) permeability of said oligonucleotide into cells, (ii) nuclease stability, or (iii) binding strength of hybridization to complementary sequences.

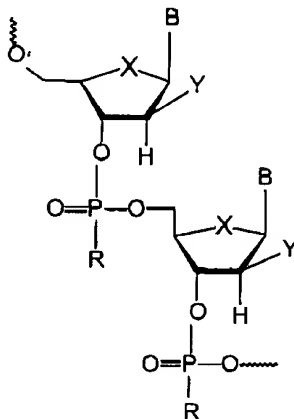
16. (Amended) A method of catalyzing chemical reactions carried out by ~~DNA~~ nucleic acid enzymes, which comprises using the composition of claim 2.

17. (Amended) The method of claim 7 ~~or 8~~ wherein said oligonucleotide is a chimera of at least one ANA oligonucleotide unit and at least one 2'F ANA oligonucleotide unit to enhance at least one of: (i) permeability of said oligonucleotide into cells, (ii) nuclease stability, or (iii) binding strength of hybridization to complementary sequences.

18. (Amended) An oligonucleotide for selectively preventing gene transcription and expression in a sequence-specific manner in a host; which comprises an oligonucleotide consisting essentially of arabinose sugars hybridizing to a single stranded RNA to induce RNase H activity; an oligonucleotide consisting essentially of arabinose sugars substituted at 2' position of the sugar ring with halogen, alkyl, alkylhalide, alkylsulfhydryl, allyl, amino, aryl, alkoxy, or azido and hybridizing to duplex DNA/DNA or DNA/RNA to

form a triple helical complex; and at least one 2-O-methyl-D-ribose sugar at 3', 5' or both terminus of said oligonucleotide.

19. (Amended) The oligonucleotide of claim 18, wherein said oligonucleotide has the formula:



wherein,

B is selected from the group consisting of adenine, guanine, uracil, thymine, cytosine, inosine, and 5-methylcytosine;

Y at the 2' position of the sugar ring is selected from the group consisting of a halogen (fluorine, chlorine, bromine, iodine), ~~hydroxyl~~, alkyl, alkylhalide (e.g., -CH₂F), alkylsulfhydryl (-SCH₃), allyl, amino, aryl, alkoxy, and azido;

R at the internucleotide phosphate linkage is selected from the group consisting of oxygen, sulfur, methyl, amino, alkylamino, dialkylamino (the alkyl group having one to about 20 carbon atoms), methoxy, and ethoxy; and

X at the furanose ring (position 4') is selected from the group consisting of oxygen, sulfur, and methylene (CH₂).